NATIONAL CENTER FOR ATMOSPHERIC RESEARCH
P. O. Box 1470 • Boulder, Colorado 80302
Telephone: (303) 494-5151 • TWX: 910-940-3245 • Telex: 45 694

2 January 1975

Professor Joshua Lederberg
Department of Genetics
Stanford University School of Medicine
Stanford, California 94305

Dear Professor Lederberg:

I would greatly appreciate your advice on two important questions regarding radiation induced mutations and cancer in man:

(1) What is the published evidence that would support the view that natural radioactivity cannot account for observed rates of mutation in living cells? In connection with an early suggestion by Hermann Muller (Amer. Nat. 64, 220, 1930) to the effect that the high spontaneous mutation rate in Drosophila could not be explained on the basis of natural radiation, I would point out that the Brownian motion of the very small airborne dust particles, to which the short-lived radioactive daughters of radon-222 are attached, may result in substantial alpha activity accumulation on Drosophila as well as on other airborne insects, bacteria and viruses. On this basis, the cumulative alpha radiation dose, principally that from ^{214}Po, may explain the observed high incidence of spontaneous mutation. I also note that seedling plants, grown from seeds stored for various periods of time, reportedly exhibit an incidence of mutations which increases with increased time of seed storage. In this case, it is conceivable that the accumulation of ^{210}Pb on the seed coverings during plant growth, the subsequent ingrowth of ^{210}Po, and the cumulative ^{210}Po alpha dose to the stored seed may explain the observations. Thus, for these two cases the processes may be analogous to those involved in the accumulation of ^{210}Pb and ^{210}Po on tobacco trichomes and insoluble cigarette smoke particles, described in the enclosed reprint. Is there any convincing evidence of spontaneous mutations not attributable to radiation? Can you please give me the references to the most recent published discussions of the adequacy of radiation as the agent of spontaneous mutations in nature.

(2) My second question concerns the availability of published evidence on the nature of the somatic cell mutations which give rise to malignant cells in mammals and man. Do they involve gene mutations alone, chromosome structural changes, or a combination of the two?

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> If one or more multiple breaks in the chromosomes of the original normal cells are essential to give rise to the structure of the product malignant cell, then it would follow that internal alpha emitters would play a very important role in the incidence of human cancer. This appears to me to be a key question relevant to assessing the relative importance of chemicals, viruses and radiation as agents of human cancer.

I would value your comments on these questions and would appreciate references to recent published discussions of them. May I also have reprints of your own recent articles bearing on these problems. Thank you.

Sincerely yours,

Edward A. Martell

Enclosure